

### Remarks

The claims in the application are claims 6, 7, 10-16, 23-26, 28 and 29. Claims 1-5, 8, 9, 17-22, and 27 have been cancelled.

The examiner has rejected claims 6, 7, 10-16 and 29 under 35 U.S.C. 102(a) as being anticipated by Alberto et al (J. Am. Chem. Soc., 1998, 120, pp. 7987-7988). By the above amendments to the claims, this rejection has been overcome. The reference does not disclose or suggest the presently claimed non-aromatic ligands to be employed in a useful imaging fluid. In fact, the reference teaches away from such ligands in the following statement from the reference found at p. 7988, second column:

“Although PADA could stabilize intermediate oxidation states (as found with its fragment imino-N,N-diacetic acid<sup>17</sup> or pyridine<sup>18</sup>), such behavior was not observed and 3 (<sup>99m</sup>Tc) formed in quantitative yield.”

In other words, the above quoted statement amounts to a teaching that imino-N,N-diacetic acid will not provide the desired form of Tc but that PADA will. The entire reference, taken as a whole is a demonstration of the surprising and novel discovery of the present inventor, i.e., that non-aromatic aminopolycarboxylates not only stabilize the desired form of Tc but also provides unexpected advantages over aromatic counterparts. The claims have now been limited to ligands having at least three carboxylate groups thereby eliminating the IDA of the reference, although such disclosure is a negative one with respect to the utility now discovered by the present inventor.

Such surprising and unexpected advantages are noted in the specification at p. 4 and also demonstrated by the data in the present application as filed. The data in Tables 3, 4 and 5 reporting the biodistribution of the Octreotate indicate a high proportion located in the kidneys

while also indicating receptor specific activity. It is particularly demonstrated in Table 5 that the kidney clearance is about doubled for the claimed compound over the prior art Histamine. This result is noted in the text of Example 6. What this data translates to is the safety and efficacy of the novel ligands. By being taken up by the kidneys there is evidence that the body will safely eliminate the radionuclide quickly and safely rather than being taken up by liver where longer disposal rates are widely known in the art.

Accordingly, not only does Alberto et al., referred to above, not teach or suggest the present invention, it actually teaches away from it and would suggest that the surprising and unexpected results now found by the present inventor should not even be investigated as such work would end in the ligand providing the wrong form of Tc (actually a mixture of undesired forms).

The present claims, as amended now avoid the prior art by eliminating IDA. It is submitted that the law as announced by the Court in the case of Application of Stemniski, 444 F. 2d 581, 585; 170 USPQ 3443, 347 (C.C.P.A. 1971), states the following:

“It is not an easy matter to determine whether we have before us a case in which the evidence adduced by the Patent Office to establish a *prima facie* case of obviousness is adequate *ab initio*, or whether the greater error lies in its failure to consider appellant’s discovery of a new and apparently unobvious usefulness for the claimed compounds as adequate rebuttal evidence of that *prima facie* case in a situation where, as here, the principal prior art neither discloses nor renders obvious a usefulness for the compounds it describes. Suffice it to say that we are convinced the board erred in sustaining the rejection under the circumstances

presented by this record. Perhaps some of that error may be attributed to this court's failure to render consistent precedent over the years."

Further, the Court in Stemniski 444 F.2d at 587 ruled that where the prior art does not disclose or suggest any usefulness for compounds and the applicant does describe a use for closely related but novel compounds, the applicant need not show that the prior art compound does not have the described use.

In view of these principles, Alberto et al. is not a viable disclosure. As noted above Alberto et al. does not disclose a viable use for NTA in this art. In fact it negates such use by its teaching.

Under the rule of Stemniski, Alberto et al. is not a viable disclosure under Section 103 and hence, does not support a rejection of obviousness because of its failure to disclose or suggest a practical use for NTA.

Accordingly, the Examiner is respectfully requested to withdraw the rejection under 35 U.S.C. 102(a) in view of the above amendments and remarks.

The Examiner has rejected claims 6, 23, 24, 26, 28, and 29 under 35 U.S.C. 103(a) as being unpatentable over Alberto et al., cited above, for reasons of record in the Office Action of Feb. 5, 2003 as well as for reasons stated in the above noted rejection under 35 U.S.C. 102(a). As noted above, not only does Alberto et al. not disclose or suggest the use of the non-aromatic ligands of the present invention, Alberto et al. teaches away from the present invention. The above remarks with respect to the rejection under 35 U.S.C. 102(a) are repeated here with respect to the rejection under 35 U.S.C. 103(a). A reference that warns not to employ ligands now claimed cannot be said to render such ligands obvious. Furthermore, the inventor now teaches a new class of ligands with unexpected advantages over ligands of the type actually taught by

Alberto. The present invention provides a new class of ligands heretofore believed to be objectionable for use as now taught. Such facts fully support the non-obviousness of the present invention. It has long been held that aromatic compounds are patentably distinct from non-aromatic compounds. The presently claimed non-aromatic compounds are therefore non-obvious over the prior art of Alberto et al. Accordingly, the Examiner is respectfully requested to withdraw the rejection claims 6, 23, 24, 26, 28, and 29 under 35 U.S.C. 103(a) on the basis of Alberto et al.

### **The New Rejection**

The Examiner, in view of applicants amendment, has newly rejected claims 6, 7, 10-16, 23, 24, 26, 28, and 29 under 35 U.S.C. 103(a) on the basis of Alberto et al. (WO 98/48848) (hereinafter referred to as "Reference I") in view of Alberto et al. (J. Am. Chem. Soc.) (hereinafter referred to as "Reference II"). This rejection is traversed for the following reasons.

While it is true that the "Reference I" does not teach or suggest the non-aromatic ligands of the present invention, it is respectfully submitted that "Reference II" does not supply such deficiency of "Reference I". "Reference II" discloses only aromatic ligands (PADA or pyridine) as being useful. As noted above, "Reference II" notes that non-aromatic ligands only stabilize "intermediate oxidation states" of Tc and such intermediate states are not what is desired in the imaging work for which the product is intended. Thus, as noted above, the secondary reference not only does not supply the deficiencies of "Reference I" but also actually teaches away from the present invention and its unexpected advantages in its use as noted above. In view of the above amendments and remarks, it is respectfully requested that the newly applied rejection be withdrawn.

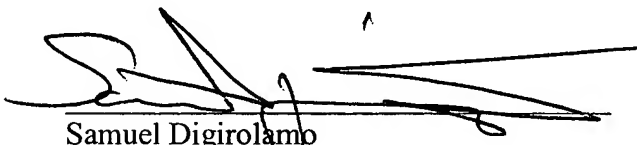
In view of the above amendments and remarks, it is respectfully requested that the Examiner allow the claims and pass the application to issue at the earliest opportunity.

It is respectfully requested that this amendment under 35 C.F.R. 116 be entered as it places the claims in condition for allowance. Alternatively, it is requested that the above amendment be entered to place the claims in better condition for appeal.

If any issue regarding the allowability of any of the pending claims in the present application could be readily resolved, or if other action could be taken to further advance this application such as an Examiner's amendment, or if the Examiner should have any questions regarding the present amendment, it is respectfully requested that the Examiner please telephone Applicant's undersigned attorney in this regard.

Respectfully submitted,

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